

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-20 (canceled)

21 (new): A method of producing a host cell capable of producing a product of interest, comprising:

(a) introducing a DNA construct into a population of host cells, wherein the DNA construct comprises, in operable linkage, a transcriptional regulatory region; a fusion gene comprising a selectable gene and an amplifiable gene; and a gene encoding the product of interest;

(b) culturing the host cell population in a selective medium, wherein the culturing is the first exposure of the host cell culture to selective conditions; and

(c) cloning a host cell from the selected host cell population, wherein the host cell is capable of producing at least about 250 mg/l of the product of interest.

22 (new): The method of claim 21, wherein the fusion gene is positioned within an intron between the transcriptional regulatory region and the gene encoding the product of interest, the intron defined by a 5' splice donor site and a 3' splice acceptor site.

23 (new): The method of claim 22, wherein the intron provides a splicing efficiency of between 80% and 99%.

24 (new): The method of claim 22, wherein the amplifiable gene is the gene encoding DHFR and the selective medium comprises at least about 25 nM methotrexate.

25 (new): The method of claim 22, wherein the amplifiable gene is the gene encoding DHFR and the selective medium comprises at least about 50 nM methotrexate.

26 (new): The method of claim 22, wherein the host cell is a mammalian cell.

- 27 (new): The method of claim 26, wherein the host cell is a CHO cell.
- 28 (new): The method of claim 22, wherein the amplifiable gene is selected from the group consisting of the gene encoding dihydrofolate reductase (DHFR) and the gene encoding glutamine synthetase.
- 29 (new): The method of claim 28, wherein the amplifiable gene is the gene encoding DHFR.
- 30 (new) The method of claim 22, wherein the selectable gene is a gene encoding puromycin resistance.
- 31 (new): The method of claim 22, wherein the fusion gene comprises a gene encoding puromycin resistance fused to a gene encoding DHFR.
- 32 (new): The method of claim 31, wherein the gene encoding puromycin resistance is 5' to the gene encoding DHFR.
- 33 (new): The method of claim 22, wherein the product of interest is a protein selected from the group consisting of an antibody, enzyme, hormone, lipoprotein, clotting factor, anti-clotting factor, cytokine, viral antigen, chimeric protein, transport protein, regulatory protein, homing receptor, and addressin; or a fragment of said protein.
- 34 (new): The method of claim 22, wherein said product of interest is a humanized antibody.
- 35 (new): The method of claim 22, wherein the DNA construct further comprises, in operable linkage, a second transcriptional regulatory region and a second gene encoding a second product of interest.
- 36 (new): A host cell produced according to the method of claim 22.

37 (new): The host cell of claim 36, wherein the amplifiable gene is the gene encoding DHFR, the selectable gene is a gene encoding puromycin resistance, and the CHO cell has a DHFR- phenotype.

38 (new): A method of producing a product of interest, comprising culturing a host cell produced according to the method of claim 22, under conditions suitable to cause expression of at least about 250 mg/l of the product of interest.

39 (new): A cell culture composition comprising a host cell produced according to claim 22 and at least about 250 mg/l of the product of interest.

40 (new): A method of producing a host cell capable of producing a product of interest comprising introducing a DNA construct into a population of host cells in suspension culture, wherein the DNA construct comprises in order from 5' to 3':

a) a transcriptional regulatory region;

b) a transcriptional initiation site;

c) a fusion gene comprising a selectable gene and an amplifiable gene, wherein the fusion gene is positioned within an intron defined by a 5' splice donor site and a 3' splice acceptor site;

d) a gene encoding the product of interest; and

e) a transcriptional termination site;

wherein the transcriptional regulatory region regulates transcription of the amplifiable gene and the gene encoding the product of interest.

41 (new): The method of claim 40, further comprising culturing the host cell population in a selective medium, wherein the culturing is the first exposure of the host cell culture to selective conditions.

42 (new): The method of claim 41, further comprising cloning a host cell from the selected host cell population, wherein the host cell is capable of producing at least about 250 mg/l of the product of interest.

43 (new): The method of claim 40, wherein the host cell is capable of producing at least about 250 mg/l of the product of interest

44 (new): The method of claim 40, wherein the host cell population is in a spinner vessel.

45 (new): The method of claim 40, wherein the host cell culture has a cell density of at least about 5×10^5 /ml.

46 (new): The method of claim 40, wherein the host cell culture has a cell density of at least about 1.5×10^5 /ml.

47 (new): The method of claim 40, wherein the amplifiable gene is the gene encoding DHFR.

48 (new): The method of claim 40, wherein the fusion gene comprises a gene encoding puromycin resistance fused to a gene encoding DHFR.

49 (new): The method of claim 48, wherein the gene encoding puromycin resistance is 5' to the gene encoding DHFR

50 (new): The method of claim 40, wherein the product of interest is selected from the group consisting of an antibody, enzyme, hormone, lipoprotein, clotting factor, anti-clotting factor, cytokine, viral antigen, chimeric protein, transport protein, regulatory protein, homing receptor, and addressin and a fragment of any of said product of interest.

51 (new): The method of claim 40, wherein the transcriptional regulatory region comprises a SV40 promoter.

52 (new): The method of claim 40, wherein the transcriptional regulatory region comprises a CMV promoter.

53 (new): The method of claim 40, wherein steps (b) and (c) are performed simultaneously.

54 (new): The method of claim 40, wherein the DNA construct further comprises, in order from 5' to 3':

- (f) a second transcriptional regulator region;
- (g) a second transcriptional initiation site;
- (h) a second product gene encoding a second product of interest; and
- (i) a transcriptional termination site;

wherein the second transcriptional regulatory region regulates transcription of the second gene encoding the second product of interest.

55 (new): A method of rapidly selecting a host cell producing a product of interest, comprising:

(a) introducing a DNA construct into a population of host cells, wherein the DNA construct comprises, in operable linkage, a transcriptional regulatory region; a fusion gene comprising a selectable gene and an amplifiable gene; and a gene encoding the product of interest;

(b) culturing the host cell population in a selective medium, wherein the culturing is the first exposure of the host cell culture to selective conditions; and

(c) cloning a host cell from the selected host cell population.

56 (new): The method of claim 55, wherein the rapid selection occurs in five to six weeks.